Tularemia Information for Professionals

Agent: *Francisella tularensis* is a small gram-negative coccobacillus. There are two main serotypes: Jellison Types A and B. Type A is considered the more virulent form. *F. tularensis* may be aerosolized in dry or wet form.

Reporting Requirements for Disease: Report any suspect cases of tularemia to your local health authority within one working day; or, call the Texas Department of State Health Services at 1-800-252-8239. Case clusters or multiple cases should be reported immediately.

Infection Control: No evidence exists for person-to-person transmission. Standard Precautions should be followed. Environmental surfaces should be decontaminated with soap and water and a hospital grade disinfectant.

Incubation Period: 2-10 days

Signs/Symptoms: Most authorities still classify tularemia into six clinical forms that loosely correlate with the usual route of exposure and presenting complaints-ulceroglandular, glandular, oculoglandular, pharyngeal, typhoidal, and pneumonic. The size of the inoculum and host response undoubtedly plays some role in the clinical presentation. However some authorities prefer to lump the six categories into two basic groups: ulceroglandular, which accounts for about three fourths of the cases (and includes all presentations with skin or mucous membrane lesions or lymph nodes ≥ 1cm) and typhoidal, which accounts for the remaining quarter.

Most patients have fever; headache, chills, cough, chest pain, sore throat, vomiting, diarrhea, anorexia, and abdominal pain are also common. Stiff neck and back pain may occur. A rash may occur in up to one third of patients and can take almost any form-maculopapular, vesiculopapular, erythema nodosum, erythema multiforme, and urticaria. Patients with **oculoglandular** tularemia present with painful, often purulent, conjunctivitis, which is associated with lymphadenopathy of the head and neck that may be preceded by photophobia and tearing. Patients with **pharyngeal** tularemia, have severe sore throat unresponsive to penicillin; and those with classic **typhoidal** tularemia, have the nonspecific symptoms described above with no localizing symptoms.

Skin lesions (**ulceroglandular**), may precede, follow, or occur concurrent to lymphadenopathy, and usually progress from a painful papule to a pustule that ulcerates with a raised border around a crater. Lymphadenopathy (**glandular**) may occur without skin lesions but with systemic symptoms. **Pneumonic** tularemia can be either primary or secondary; secondary pneumonia is particularly likely to accompany primary pharyngeal or classic typhoidal (ie, no obvious focus). Patients with pneumonic tularemia usually have a dry nonproductive cough, dyspnea, pleuritic chest pain, and fever. Physical examination may be nonspecific or reveal rales, a friction rub, or signs of consolidation or effusion. Symptoms common to all forms include fever; headache, chills, cough, chest pain, sore throat, vomiting, diarrhea, anorexia, and

abdominal pain, with stiff neck and back pain occurring less frequently. A rash occurs in about one third of patients varying from maculopapular, vesiculopapular, erythema nodosum, erythema multiforme, to urticaria.

Diagnosis: **Oculoglandular** tularemia should be differentiated from bacterial and adenoviral eye infections. Because of the nonspecific symptoms associated with **typhoidal** tularemia, the differential diagnosis is broad and includes collagen-vascular diseases, neoplasms, and drug reactions as well as the infectious agents specifically associated with typhoid fever, tuberculosis, relapsing fever and more generally with abscesses, osteomyelitis, and endocarditis.

Pneumonic tularemia should be differentiated from common causes of pneumonia such as infection with *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Streptococcus pneumoniae* as well as rare causes of pneumonia such as *Coxiella burnetii*, *Chlamydia psittaci*, *Mycobacterium tuberculosis*, and the mycoses. Large numbers of patients presenting with similar systemic illnesses, in which a portion have a nonproductive pneumonia may be indicative of tularemia.

Diagnostic Tests: The organisms can be isolated or detected by PCR from blood, ulcers, conjunctival exudates, sputum, gastric washings, and pharyngeal exudates. Gram stain of smears or biopsies is rarely useful. Culture is hazardous to laboratory personnel and is technically difficult, particularly after institution of appropriate antibiotic therapy. Fourfold increase in tube agglutination or microagglutination titer is diagnostic of infection. Titers are usually negative during the first week of infection, positive in 50-70% of cases in the second week, and reach a maximum in 4-8 weeks. Cross-agglutination can occur with *Brucella* and *Proteus* species.

Specimen Submission: All specimens must be triple contained in an approved shipping container and have biohazard labels. Before transport is arranged, the receiving laboratory must be alerted prior to transport by calling (800) 252-8239 ("press 1"). Newly available diagnostic tests may be discussed at that time. Isolation is a significant laboratory hazard and must be performed in BSL-3 containment. Specimens must be accompanied by a Specimen Submission Form (G-1A) and submitted to the Texas Department of State Health Services Laboratory, 1100 West 49th Street, Austin, TX 78756. Tularemia should be prominently mentioned on the G-1A so that appropriate biosafety precautions will be taken in the laboratory.

Additional Tests: Routine examination of the sputum is not helpful, however a false-positive direct fluorescent antibody stain for *Legionella* on bronchoscopy specimens has been reported. Infected pleural fluid is exudative, negative on Gram stain, and usually contains more than 1000 leukocytes/mm3; cells are predominantly lymphocytes, but neutrophilic effusions may occur.

Secondary pleuropulmonary involvement is common in typhoidal cases, with pleural effusions or pulmonary infiltrates being present in up to 45% of patients. In patients with the pneumonic form of disease, 25-30% will have radiographic infiltrates without any clinical findings of pneumonia. White blood cell count and sedimentation rate may be normal or elevated. Thrombocytopenia, hyponatremia,

elevated serum transaminase, increased creatine phosphokinase, myoglobinuria and sterile pyuria are sometimes present.

Radiological evidence of pneumonia or mediastinal lymphadenopathy is usually evident. Acute radiographic changes may include subsegmental or lobar infiltrates, hilar adenopathy, pleural effusion, and apical or miliary infiltrates. Less common changes include ovoid densities, cavitation, and bronchopleural fistula.

Treatment: Adults: Streptomycin 1 g IM 8-12 hours for 10 days, or gentamicin 5 mg/kg IM or IV for 10 days. Children: Streptomycin 15 mg/kg IM q 12 hours (should not exceed 2 g/d) for 10 days or gentamicin 2.5 mg/kg IM or IV q 8 hours for 10 days.

Prophylaxis: Adults: Doxycycline 100 mg q12h po for 14 days, or ciprofloxacin 500 mg q 12 hours po for 14 days. Children: Doxyclycline; if 45 ≥ kg, give 100 mg po q 12 hours; if < 45 kg, give 2.2 mg/kg po q 12 hours for 14 days or ciprofloxacin 15 mg/kg po q 12 hours for 14 days (not to exceed 1 g per day).